ammonium hydroxide (112 mL). After 30 min, the reaction is concentrated under reduced pressure (below 30 °C) followed by coevaporation with toluene (2x100 mL). The residue is dissolved in ethyl acetate-methanol (400 mL, 9:1) and the undesired silyl by-products are removed by filtration. The filtrate is concentrated under reduced pressure and purified by silica gel flash column chromatography (800 g, chloroform-methanol 9:1). Selected fractions are combined, concentrated under reduced pressure and dried at 25 °C/0.2 mmHg for 2 h to give the title compound.

EXAMPLE 84

N^6-Benzoyl-5'-O-(dimethoxytrityl)-2'-*O*-(*trans*-2-methoxycyclohexyl) adenosine

[0266] A solution of N^6-benzoyl-2'-*O*-(*trans*-2-methoxycyclohexyl) adenosine (0.285 mol) in pyridine (100 mL) is evaporated under reduced pressure to an oil. The residue is redissolved in dry pyridine (300 mL) and 4,4'-dimethoxytriphenylmethyl chloride (DMT-Cl, 10.9 g, 95%, 0.31 mol) added. The mixture is stirred at 25 °C for 16 h and then poured onto a solution of sodium bicarbonate (20 g) in ice water (500 mL). The product is extracted with ethyl acetate (2x150 mL). The organic layer is washed with brine (50 mL), dried over sodium sulfate (powdered) and evaporated under reduced pressure (below 40 °C). The residue is chromatographed on silica gel (400 g, ethyl acetate-hexane 1:1. Selected fractions were combined, concentrated under reduced pressure and dried at 25 °C/0.2 mmHg to give the title compound.

EXAMPLE 85

[N^6-Benzoyl-5'-*O*-(4,4'-dimethoxytrityl)-2'-*O*-(*trans*-2-methoxycyclohexyl) adenosine-3'-O-yl]-N,N-diisopropylamino-cyanoethoxy phosphoramidite

[0267] Phosphitylation of N^6-benzoyl-5'-O-(dimethoxytrityl)-2'-*O*-(*trans*-2-methoxycyclohexyl) adenosine was performed as illustrated above to give the title compound.

EXAMPLE 86

General procedures for chimeric C3'-endo and C2'-endo modified oligonucleotide synthesis

[0268] Oligonucleotides are synthesized on a PerSeptive Biosystems Expedite 8901 Nucleic Acid Synthesis System. Multiple 1-mmol syntheses are performed for each oligonucleotide. The 3'-end nucleoside containing solid support is loaded into the column. Trityl groups are removed with trichloroacetic acid (975 mL over one minute) followed by an acetonitrile wash. The oligonucleotide is built using a modified diester (P=O) or thioate (P=S) protocol.

Phosphodiester protocol

[0269] All standard amidites (0.1 M) are coupled over a 1.5 minute time frame, delivering 105 μL material. All novel amidites are dissolved in dry acetonitrile (100 mg of amidite/1 mL acetonitrile) to give approximately 0.08-0.1 M solutions. The 2'-modified amidites (both ribo and arabino monomers) are double coupled using 210 μL over a total of 5 minutes. Total coupling time is approximately 5 minutes (210 mL of amidite delivered). 1-H-tetrazole in acetonitrile is used as the activating agent. Excess amidite is washed away with acetonitrile. (1S)-(+)-(10-camphorsulfonyl) oxaziridine (CSO, 1.0 g CSO/8.72 mL dry acetonitrile) is used to oxidize (3 minute wait step) delivering approximately 375 μL of oxidizer. Standard amidites are delivered (210 μL) over a 3-minute period.

Phosphorothioate protocol

[0270] The 2'-modified amidite is double coupled using 210 μL over a total of 5 minutes. The amount of oxidizer, 3H-1,2-benzodithiole-3-one-1,1-dioxide (Beaucage reagent, 3.4 g Beaucage reagent/200 mL acetonitrile), is 225 μL (one minute wait step). The unreacted nucleoside is capped with a 50:50 mixture of tetrahydrofuran/acetic anhydride and tetrahydrofuran/pyridine/1-methyl imidazole. Trityl yields are followed by the trityl monitor during the duration of the synthesis. The final DMT group is left intact. After the synthesis, the contents of the synthesis cartridge (1 mmole) is transferred to a Pyrex vial and the oligonucleotide is cleaved from the controlled pore glass (CPG) using 30% ammonium

hydroxide (NH_4OH, 5 mL) for approximately 16 hours at 55 °C.

Oligonucleotide Purification

[0271] After the deprotection step, the samples are filtered from CPG using Gelman 0.45 μm nylon acrodisc syringe filters. Excess NH_4OH is evaporated away in a Savant AS160 automatic speed vac. The crude yield is measured on a Hewlett Packard 8452A Diode Array Spectrophotometer at 260 nm. Crude samples are then analyzed by mass spectrometry (MS) on a Hewlett Packard electrospray mass spectrometer. Trityl-on oligonucleotides are purified by reverse phase preparative high performance liquid chromatography (HPLC). HPLC conditions are as follows: Waters 600E with 991 detector; Waters Delta Pak C4 column (7.8X300mm); Solvent A: 50 mM triethylammonium acetate (TEA-Ac), pH 7.0; Solvent B: 100% acetonitrile; 2.5 mL/min flow rate; Gradient: 5% B for first five minutes with linear increase in B to 60% during the next 55 minutes. Fractions containing the desired product/s (retention time = 41 minutes for DMT-ON-16314; retention time = 42.5 minutes for DMT-ON-16315) are collected and the solvent is dried off in the speed vac. Oligonucleotides are detritylated in 80% acetic acid for approximately 60 minutes and lyophilized again. Free trityl and excess salt are removed by passing detritylated oligonucleotides through Sephadex G-25 (size exclusion chromatography) and collecting appropriate samples through a Pharmacia fraction collector. The solvent is again evaporated away in a speed vac. Purified oligonucleotides are then analyzed for purity by CGE, HPLC (flow rate: 1.5 mL/min; Waters Delta Pak C4 column, 3.9X300mm), and MS. The final yield is determined by spectrophotometer at 260 nm.

PROCEDURES

PROCEDURE 1

ICAM-1 Expression

Oligonucleotide Treatment of HUVECs

[0272] Cells were washed three times with Opti-MEM (Life Technologies, Inc.) prewarmed to 37 °C. Oligonucleotides were premixed with 10 g/mL Lipofectin (Life